with back-pressure regulation." Support for these amendments is found in the specification at, for example, page 5, lines 1-9, in the Example, in figure 2, and in original claim 2. *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claims 7 and 8 have been canceled, without prejudice.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Obviousness Rejection

Claims 1-8 were rejected solely under 35 USC §103(a) as being unpatentable over Zhang *et al.*, (CA 113:198104, abstract of Zhongguo Yiyao Gongye Zazhi (1990), 21(6), 256-61) ("Zhang") in view of Lee *et al*, (CA 124:105153, abstract of J. Microcolumn Sep. (1995), 7(5), 477-83) ("Lee"). (Paper No. 17 at 2).

For the reasons set forth below the rejection, respectfully is traversed.

Zhang discloses "HPLC determination of vitamin D_3 preparation." (Title). The Abstract relied on by the rejection discloses the following:

> In the column system suitability test following irradn. of heated vitamin D_3 soln. by UV with main wave length 254 and 365 nm for 5 min, 6 isomers were sepd. with the ***normal-phase HPLC*** (Waters Resolve Silica column, 0.3% n-pentanol in hexane as mobile phase, detected at 254 nm), with resoln. factor, R, >1.0. The linearity was obtained in 0.5-60 .mu.g vitamin D_3. The low concn. (1ppm) prepn. could be detd. by internal (di-Me phthalate) method or external (thermal equil.) method with error 10%. The error in detn. of high-concn. prepn. was 3%. (Abstract).

Lee discloses the use of an "enhanced-fluidity" or a low viscosity liquid mobile phase as an eluent in ***reversed phase HPLC***. (Page 477, Col. 1). In Lee, "***all***" experiments

disclosed were performed using a 0.7/0.30 mole fraction methanol/H_2O mixture or a 0.49/0.21/0.30 mole fraction methanol/H_2O/CO_2 mixture." (Page 478, Col. 1).

The Examiner has apparently maintained the rejection found in the Office Action dated April 9, 2001. (Paper 15). Accordingly, the rejection found in Paper 15 is addressed below.

In making the rejection, the Examiner asserted that Zhang "teaches the separation of 6 isomers separated by using irradiation technique and the purification on silica column (stationary phase)." (Paper No. 15 at 3). The Examiner acknowledged, however, that the "[i]nstant claims differ from [Zhang] in claiming the liquid CO_2 for separation by column chromatography using liquid CO_2." (*Id.*). To fill the acknowledged gap, the Examiner relied upon Lee as "teaching the separation of coal tar vitamins and other related compounds. The enhance[d] fluidity liquid mobile phase containing ***CO_2/methanol/water*** are used in a column." (*Id.*).

The Examiner asserted that the "references are combinable because they are from the same field of endeavor." (*Id.*). The Examiner then contended that "[i]t would have been obvious to one skilled in the art to combine the teachings of prior art supra to separate the vitamin D derivatives particularly when Zhang *et al.* teaches irradiation technique and the purification on silica column (stationary phase) and Lee *et al.* teaches the use of liquid CO_2 for separation." (*Id.* at 4). The Examiner further contended that "ample motivation" for separating vitamin D_3 as claimed is found in the prior art, and that there was "nothing unobvious" about the process for separating the vitamin D_3 as claimed. (*Id.*).

The present claims, as amended, recite a "supercritical carbon dioxide" mobile phase. Neither Zhang nor Lee disclose the use of supercritical carbon dioxide. Lee specifically discloses a methanol/H_2O or methanol/H_2O/CO_2 liquid mobile phase. (Pg. 478, Col. 1).

Additionally, the claims recite "back-pressure regulation" and are drawn to a supercritical fluid chromatography ("SFC") process. In contrast, both Zhang and Lee disclose a HPLC technique. In fact, Lee specifically contrasts its HPLC method with SFC methods.

> The low viscosities of supercritical fluid mobile phases result in increased solute diffusion, faster speed of analysis, and lower pressure drops across the chromatographic column in SFC than in HPLC. The low column pressure drop has facilitated the use of long and/or coupled columns in packed-column SFC to increase the total number of theoretical plates for separation of complex mixtures.
>
> We have demonstrated the use of enhanced-fluidity (or low viscosity) liquid mobile phases as eluents in reverse-phased HPLC.

(Pg. 477, Col. 1).

The claims, as amended, recite supercritical carbon dioxide, and are drawn to a supercritical fluid chromatography process. The Zhang and Lee documents do not disclose or suggest the use of supercritical CO_2 as a mobile phase or the use of SFC. In sum, the present process is a supercritical fluid chromatography process utilizing a ***compressed gas*** as the mobile phase. Both Zhang and Lee rely on HPLC as the separation technique. (See Zhang Abstract and Lee at pg. 477, Col. 1). As is fundamental, the mobile phase for the HPLC processes of both Zhang and Lee is a ***liquid***. In view of the foregoing, the rejection has been rendered moot, and should be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejection, and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Box AF, Commissioner for Patents, Washington, D.C. 20231, on December 5, 2001.

Stephen J. Brown, Reg. No. 43,519

Respectfully submitted,

By: _____

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"Marked Up" Replacement Paragraph Pursuant to Rule 1.121(b)

An apparatus from the Hewlett Packard company (HP G1205A SFC) is used for the investigation of the chromatographic production of the components, particularly of vitamin D_3 or previtamin D_3, from an isomer mixture. The apparatus consists of the basic units comprising pump, oven with gas phase detector, external detector and automatic sampler. A flow diagram of the apparatus is shown in Fig. 2 [3]. The apparatus is supplied continuously with liquid carbon dioxide. Depending on the chosen pressure and temperature conditions, the mobile phase can be operated in the supercritical range (above about 31°C ansd 7.3 MPa in the case of pure CO_2) or in the subcritical range.

In re Application of : Monika JOHANNSEN
U.S. Serial No.: 09/335,022
For: **PROCESS FOR PRODUCING VITAMIN D_3 AND PREVITAMIN D_3**

"Marked Up" Amendment to Claim 1 Pursuant to Rule 1.121(c)

1. (Thrice Amended) A process for the isolation of vitamin D_3 previtamin D_3 from a mixture containing vitamin D_3 or previtamin D_3, which process comprises separating the vitamin D_3 or previtamin D_3 by a normal phase column chromatographic technique with back-pressure regulation, wherein a mobile phase of the chromatography comprises supercritical carbon dioxide [or liquid carbon dioxide].